

Remarks

Claims 1, 3-10, and 16-23 are pending and under consideration by the Examiner in this Application. Claims 2 and 11-15 were previously canceled. Claims 1, 3-10, 16-20, 22, and 23 have been amended to correct typographical errors. Applicant submits that no new matter has been added to the Application by this Amendment.

Each of the rejections levied in the outstanding Office Action is addressed individually below.

Rejection under 35 U.S.C. § 103

Claims 1, 3-10, and 16-23 remain rejected by the Examiner under 35 USC § 103(a) as being obvious over Oeltgen *et al.*, U.S. 6,645,938 (“Oeltgen”), in view of Motterlini *et al.*, *Circ. Res.*, 2002, 90, e17-e24 (“Motterlini.”)

Oeltgen teaches methods of preventing damage to isolated organs by exposing the organs to a preservative solution containing an effective amount of “compound-D,” a peptide of a particular sequence (SEQ ID NO: 1 in Oeltgen), which does *not* release carbon monoxide but acts in a completely different manner. The Examiner admits that Oeltgen does not teach a preservative solution containing a metal carbonyl compound which releases carbon monoxide. The Examiner alleges that “this deficiency is cured by the teachings of Motterlini *et al.*,” which teach metal carbonyl compounds which release carbon monoxide. However, Applicant respectfully submits that the Examiner has provided no teaching or suggestion as to why one of ordinary skill in the art would substitute a metal carbonyl compound for the peptide “compound-D” in the preservative solution taught by Oeltgen.

The Federal Circuit in *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991) held that “where claimed subject matter has been rejected as obvious in view of a combination of prior art references, a proper analysis under § 103 requires, *inter alia*, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success.” These two factors are deficient in the Examiner’s analysis as indicated below.

Therefore, Applicant respectfully submits that the Examiner has not established a *prima facie* case of obviousness because the Examiner merely provides conclusory statements rather than indicating, as is required, a teaching or suggestion to combine Oeltgen with Motterlini based upon some rational underpinning. The Supreme Court stated in *KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. 398 (2007), that an obviousness analysis “should be made explicit. See *In re Kahn*, 441 F.3d 977, 988 (CA Fed. 2006) (“[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness”).” The Examiner has not provided explicit rationale as to why one of ordinary skill in the art would substitute “compound-D” with a metal carbonyl compound. Furthermore, the Examiner’s rejection is without merit because one of ordinary skill in the art would not have a reasonable expectation of success in arriving at the claimed invention by combining the cited references.

The Examiner alleges “[i]t would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Oeltgen *et al.* with Motterlini *et al.* One would have been motivated to do so because Motterlini *et al.* teaches that the *transition metal carbonyls* taught are useful for defence against ischemia-reperfusion and, therefore, adding such a compound to the solution taught by Oeltgen would enhance the protective activity of the solution” (emphasis added). The Examiner’s logic is incorrect and lacks a rational underpinning as required by law. Motterlini teaches in the introductory paragraph that the HO-1 enzyme, not transition metal carbonyl complexes, are useful for protecting against ischemia-reperfusion damage: “HO-1 represents a pivotal inducible defensive system against stressful stimuli, including UVA radiation, carcinogens, ischemia-reperfusion damage, endotoxic shock, and several other conditions characterized by production of oxygen-derived free radicals.”

The Examiner broadens the subject of this passage regarding the HO-1 enzyme to generally encompass CO-releasing molecules, including transition metal carbonyls, without providing any support in Motterlini. Instead, the Examiner merely states his own conclusory position. “It is the Examiner’s position that the Motterlini teach that HO-1 results in the formation of CO and that it is pivotal in the protection of ischemic-reperfusion damage. Motterlini further teach that the HO[-1] derived CO has cytoprotective activity. *It is the Examiner’s position* that these teachings indicate *CO-releasing molecules in general* have ischemia-reperfusion protective activity” (emphasis

added). The Examiner's position is not a reasonable interpretation of Motterlini. HO-1 is a protein, *not* a transition metal carbonyl complex. As one of ordinary skill in the art would know, statements about proteins cannot be generalized to transition metal complexes. Motterlini's discussion of HO-1 is not intended to encompass CO-releasing molecules in general or transition metal carbonyl complexes in particular as the Examiner suggests.

Further, The Examiner's position regarding "ischemic-reperfusion damage" is also misleading. Motterlini implicates HO-1 in the body's defense against a broad range of "stressful stimuli, including UVA radiation, carcinogens, ischemia-reperfusion damage, endotoxic shock, and several other conditions characterized by production of oxygen-derived free radicals." There is no basis in this passage, or in all of Motterlini, to reasonably assume, as does the Examiner, that transition metal carbonyl complexes have protective activity against any one of these stressful stimuli including carcinogens, UVA radiation, endotoxic shock, or *ischemia-reperfusion damage*. Contrary to the Examiner's position, Motterlini does not teach or suggest that transition metal carbonyl complexes have protective activity against ischemia-reperfusion damage. Applicant notes, however, that even if Motterlini did teach that transition metal carbonyl complexes have protective activity against ischemia-reperfusion damage, such a teaching would still not provide a reasonable basis to combine Motterlini with Oeltgen. Oeltgen teaches peptide preservatives to protect extracorporeal or isolated organs. Motterlini does not teach or suggest, in any way, the protection of extracorporeal or isolated organs. In conclusion, there is no reasonable basis to combine Motterlini with Oeltgen. Accordingly, the Examiner has not provided a teaching or suggestion to combine Oeltgen with Motterlini based upon some explicit rational underpinning.

In addition, neither reference indicates that those of ordinary skill would have a reasonable expectation of success in making the claimed invention from the combination of Oeltgen and Motterlini. The claimed invention is directed to a new use of metal carbonyl compounds which release carbon monoxide for the protection of an extracorporeal or isolated organ. Motterlini is directed to CO-releasing molecules, but not to the protection of an extracorporeal or isolated organ. Oeltgen is directed to the protection of an extracorporeal or isolated organ with a peptide, but not with CO-releasing transition metal carbonyl complexes. It logically follows that the Examiner's combination of Oeltgen with Motterlini does not correspond to the claimed invention: "Motterlini *et al.* teaches that the transition metal carbonyls taught are useful for defence against ischemia-

reperfusion damage and, therefore, adding such a compound to the solution taught by Oeltgen would enhance the protective activity of the solution.” The claimed invention is not a combination of “compound-D” and transition metal carbonyl complexes as suggested by the Examiner.

Applicant maintains that the Examiner has not established a *prima facie* case of obviousness because the Examiner merely provides conclusory statements rather than indicating, as is required, a teaching or suggestion to combine Oeltgen with Motterlini based upon some rational underpinning. Applicant, therefore, respectfully requests the removal of this rejection under § 103.

In view of the above Remarks, Applicant believes the pending application is now in condition for allowance. Please charge any unpaid fees associated with this Response, or credit any overpayments, to our Deposit Account No. 23/2825, under Docket No. H0817.70001US00, from which the undersigned is authorized to draw.

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Respectfully submitted,

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